REMARKS

The present paper is filed in response to a FINAL office action dated January 26, 2012. This response is timely filed on May 25, 2012 by virtue of the attached petition and fee for a one-month extension of time to respond. The instant response is accompanied by a request and fee for continued examination.

As an initial matter Applicants appreciate that the previous rejections have been withdrawn and the claims have been newly rejected in view of an additional reference. To the extent that certain of the characterizations of the prior art that applications previously provided also are applicable here, those characterizations and arguments are introduced herein to overcome the rejections based on the new combination fo references.

Status of Claims

Claims 97, 157-182, 185, 186 and 188 are pending. Of these claims, claim 176 is withdrawn. Claims 97, 157-175, 177-182, 185, 186 and 188 are rejected under 35 USC 102(e) and/or USC 102(a) and also under USC 103(a). Applicants respectfully request reconsideration.

Rejection under 35 USC 102(e)/102(a)

Claims 166, 169-170, 174-175, 179-180, 185 and 188 were rejected over newly cited reference Chetverin US Patent No. 6,103,463 and/or WO 93/17126 which is the PCT counterpart of the US Patent. The US Patent is cited as allegedly anticipatory under 35 USC 102(e) and the counterpart PCT is used as a reference under 35 USC

102(a). Applicants respectfully traverse both rejections and request reconsideration in view of the following remarks.

In particular, the Office action pointed to Col. 30, lines 38-46 and Col. 33 lines 15-27 and Figure 4 to support the position that Chetverin teaches a solid array or arrays that are separated by physical barriers to permit parallel reacts and/or probe transfer wherein each array has different oligonucleotides. Applicants respectfully disagree with the Examiner's characterization of Chetverin. In Figure 7, the array of arrays is described as "a sheet on which miniature survey arrays have been 'printed' in a pattern that coincides with the arrangement of wells in the partialing array". The paragraph goes on to state that "the partialing array **31** comprising an array of wells, **31a**, is surveyed using sheet **42** having corresponds to the pattern of wells **31a**" (Col. 33 lines 20-27).

Applicants submit that the only array of arrays shown in the above quoted section from column 33 is the surveying sheet. It is clear from the description as well as the Figure shown in Figure 7 has no physical barriers between each of the arrays on the sheet. The pattern of wells that the array interrogates includes physical barriers but each well does not constitute an array.

As explained in the previous response, the claims of the present application are directed to support comprising an array of microchips immobilized on said support, each of said microchips comprising an array of oligonucleotide probes immobilized on the surface of each of said microchips to permit parallel execution of reactions. This is facilitated by the presence of a physical barrier or a hydrophobic surface that separates

each microchips from each other microchip. Thus, in order to effectively achieve parallel reactions on the same array of arrays, the arrays are separated by distinct barriers. Applicants submit that because neither of the Chetvrin documents presents any disclosure of barriers on the sheet of miniature survey arrays, those documents do not anticipate the present claims.

Applicants respectfully request reconsideration of the rejection under 35 USC 102(e)/102(a) based on Chetvrin.

Rejection under 35 USC 103(a)

Claims 97, 159-160, 163-166, 169-171, 173-175, 177-182, 185-186 and 188 are rejected under 35 USC 103(a) over a combination of Southern et al (Genomics 1992) and Chetverin (US Patent 6,103,463).

Southern was also the primary reference in a prior rejection of the claims. The combination of Southern with Chetverin again fails to establish obviousness of the present claims. As noted previously, Figure 3 of Southern merely shows an arrangement of 4 arrays of oligonucleotides but each array is identical in terms of the oligonucleotides that are attached to each array so that replicate measurements of the same reaction are taken on the four arrays. There is no barrier or other manner of containing the reaction mixtures so that different hybridization reactions using different labeled probes can be conducted on the separate individual unit arrays of Southern. The arrays of Southern simply lack separation of the unit arrays which permit separate and parallel execution of sequencing reactions and hence any attempt to perform such

multiple reactions on the Southern array would not be effective because the reaction mixture from one array would bleed into another and obscure the results obtained.

As explained above Chetverin also fails to describe any configuration of an array of arrays that includes physical barriers between the arrays. In this regard, there is little difference between the four quadrants of Southern as compared to the sheet of miniature survey arrays of Chetverin because both the Southern quadrants and the Chetverin survey arrays are presented on a sheet with no physical or hydrophobic barrier separation between the four Southern quadrants and the individual Chetverin survey arrays.

The skilled person would thus not be motivated to combine Southern with Chetverin because both methods would fail to keep the reaction mixtures separate and yet still be carried out on the survey array of Chetverin or the quadrants of Southern. This has nothing to do with sequencing oligonucleotides. Thus, Applicants request reconsideration of the rejection based on the combination of Sourthern and Chetverin.

Claims 157-158 and 167-168 were rejected under 35 USC 103(a) over a combination of Southern et al (Genomics 1992) and Chetverin (US Patent 6,103,463) and further in view of Kauver et al (US Patent 5,365,784) and/or Wang et al (US Patent 4,618,475). Applicants again traverse the rejection.

Wang again is simply related to creating a matrix with a barrier pad in it that is impregnated with hydrophobic material. There is nothing in Wang that shows why doing so would lead to a better hybridization array of Southern. Southern adequately

achieved sequencing of a small target nucleic acid in a particular type of sequencing by hybridization reaction. Use of the four arrays was to increase region specific signal detection using the same reaction conditions for all four arrays. Southern was not concerned with needing to perform multiple hybridization reactions in parallel using different sets of probes on the same array and hence Southern did not require separation of the arrays. Indeed, separating the arrays of Southern would have created an impediment or delay in the assay in that same reaction mixture would have to be supplied in four steps to the four separate arrays. Chetverin also does not include barriers for separation of the arrays and instead relies on the reaction mixtures being presented in different wells. Given the separation of Chetverin's arrays is achieved by using them with the wells shown in Figure 7 of that reference, there would be no need to separate Chetverin arrays using the teachings of Wang.

The combination of Southern and Chetverin with Kauver also fails to render obvious the presently claimed invention. As previously explained, Kauver is related to measuring methyl mannose and its binding to Conconavalin A. That discussion is irrelevant to the present invention which is used to measure different oligonucleotides which have different structures from each other. For Kauver's measurement of a single molecule there is no need to separate out the methyl mannose into separate arrays for separate reactions because all of the methyl mannose will have the same structure. As noted above, Southern is an arrangement of 4 arrays of oligonucleotides but each array is identical in terms of the oligonucleotides that are attached to each array to facilitate replicate measurements of the same reaction to be taken on all four arrays using the same reaction mixture. There is no barrier or other manner of containing the reaction

mixtures so that different hybridization reactions using different labeled probes can on the separate individual unit arrays of Southern. The arrays of Southern simply lack separation of the unit arrays which permit separate and parallel execution of sequencing reactions and hence any attempt to perform such multiple reactions on the Southern array would not be effective because the reaction mixture from one array would bleed into another and obscure the results obtained. Chetverin also fails to include barriers on its survey arrays and instead uses wells of reaction mixtures to separate the reactions – thus the reaction mixtures of Chetverin are not accomplished on the survey array but must be performed on a separate microtiter well plate.

The skilled person would not be motivated to combine Kauver with Southern because Kauver is directed at increasing the sensitivity of binding of a single sugar moiety of known structure to a lectin. This has nothing to do with sequencing oligonucleotides. There is nothing in Kauver that suggests that a platform used to detect sugars would be useful for detecting oligonucleotides. The two endeavors (detection of a sugar using conconavalin A versus determining the structure of an oligonucleotide by hybridizing it to a complementary oligonucleotide probe) are two different fields of endeavor and there is no teaching in Kauver that the methods used in the detection of a sugar are applicable to techniques of sequencing. Southern is concerned with sequencing (i.e., determining the structure of) a target nucleic acid sequence of unknown structure by determining which known counterpart nucleic acid the unknown target sequence binds to. The binding only happens where there is complementarity between the target sequence and the oligonucleotide probe. Likewise, the survey arrays of Chetverin are nucleic acid arrays. The technical field of Kauver is

different from that of Southern and Chetverin and the mere fact that Kauver asserts that it has an interest in region-specific signal detection for "convenience and simplicity of interpreting results" does not overcome the fact that Kauver already knows the identity of the thing being detected and the method of Kauver provides no structural information about the mannose detected. This argument while relating to the use of the Southern arrays as compared to Kauver is central to the differences in format of the Southern array and Kauver technique and why it is not necessarily predictable that a teaching from Kauver should be imported into the teaching of Southern and Chetverin without some nexus between the two.

In view of the above remarks Applicants believe the rejection should be withdrawn and respectfully request reconsideration of the claims for allowance.

The Commissioner is authorized to charge any additional fees or credit any overpayment to the Deposit Account of McAndrews, Held & Malloy, Account No. 13-0017.

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Respectfully submitted,

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